

REMARKS

This amendment is in response to the Final Office Action mailed June 05, 2007.

Claims 10, 11, 39-43, 48, 124-130, and 135-180 are pending in the application. Claims 39-43, 156-168, 174, 176, 178, and 180 are withdrawn from consideration. Claims 48, 124-130 and 181-196 are rejected. Claims 10, 11, 135-155, 169-173, 175, 177, 179 and 197 are allowed.

Interview Summary

Applicants thank Examiner Erez for the courtesy of an interview on June 11, 2007. The rejections in the Final Office Action of June 05, 2007 were discussed. Applicants' representatives, William L. Leschensky and Barry J. Swanson, described the distinctions between the limitations of the claimed invention and the cited art, including U.S. Patent No. 5,146,915, to Montgomery, and U.S. Patent No. 5,388,574, to Ingebrethsen. Specific limitations were discussed with respect to certain claims that would better define the claimed invention and overcome the prior art rejection.

Election/Restrictions

The Examiner notes that claims 39-43, 156-168, 174, 176, 178 and 180 drawn to an invention nonelected with traverse in the reply filed June 23, 2006 and states that a complete reply to the final rejection must include cancellation of the nonelected claims or other appropriate action. Office Action at 2. Accordingly, Applicants have cancelled claims 39-43, 156-168, 174, 176, 178 and 180.

Amendments to the Claims

Without prejudice to the Applicants' rights to present claims of equal scope in a timely filed continuing application, to expedite prosecution and issuance of the application, the Applicants have amended claims 10, 48, 124, 130, 139, 184, 185 and 191 and cancelled claims 39-43, 140-144, 146, 147, 154, 156-170, 174-180 and 192-197. The Applicants have also presented new claims 198-209. The amended claims and the new claims are supported by the specification. The amendments to the claims do not introduce new matter. Applicants respectfully submit that the amendments to the claims put the case in condition for allowance.

The Examiner is respectfully requested to enter the amendments to the claims and allow all amended claims.

Claim Rejections Under 35 USC § 102

Claim 48 is rejected under 35 USC § 102(b) as being anticipated by U.S. Patent No. 5,146,915, to Montgomery (“Montgomery”). Montgomery pertains to an anesthetic vaporizer for use with anesthetic agents having low boiling points (Montgomery, abstract). The Examiner cites Montgomery as teaching “a method of generating an aerosol comprising the steps of heating a physiologically active compound via heaters 32 to vaporize the compound within chamber 12. The vapor generated by the heaters are then mixed with a carrier gas (col. 2, lines 8-10) to form a ratio of vapor to carrier gas when a stable concentration of particles in the gas is reached.” Office Action at 2.

Applicants respectfully disagree in view of the elements of claim 48 and the disclosure of Montgomery. Claim 48 requires the step of “cooling the resulting vapor by mixing the vapor with a gas in a predetermined ratio, selected to form an aerosol having a desired particle size when a stable concentration of particles is reached.” This limitation clearly distinguishes Applicants’ claimed invention from the vaporizer disclosed by Montgomery.

Claim 48 is directed to “[a] method for generating an aerosol” and requires “form[ing] an aerosol.” As set forth in the present specification, “[a]n aerosol is defined as an assembly of liquid or solid particles suspended in a gaseous medium” (Specification at page 1, lines 15-17; *citing* Aerosol Measurement, Willeke and Baron, Wiley-Interscience, 1993). By contrast, Montgomery discloses delivery of a gas to a patient (*i.e.*, a gaseous anesthetic agent contained within a carrier gas). *See, e.g.*, Montgomery, col. 2, lines 62-65 (referring to “the concentration of gaseous anesthetic agent in the carrier gas leaving the outlet”) (emphasis added). Nowhere does Montgomery disclose an aerosol, how to make an aerosol, or any assembly of liquid or solid particles, their size or stability of their concentration. Thus, Montgomery fails to teach or suggest “form[ing] an aerosol” as required by claim 48. For this reason alone, the present invention is not anticipated by Montgomery.

In addition, Montgomery fails to teach or suggest “cooling the resulting vapor by mixing the vapor with a gas” as required by claim 48. In fact, Montgomery teaches that the vapor should not be cooled. Montgomery states that “the heater 32 is positioned within the vaporizer

so that, in addition to the vaporizing chamber 12, the passageways 6, 10, 26 and regulator 14 are also heated to prevent the anesthetic condensing out on the walls of the vaporizer which would otherwise be cooler than the vaporizing chamber” (Montgomery, col. 3, lines 19-25).

The Examiner points out that “[t]he embodiment of Fig. 3 does not have any heaters in the passageways 6, 19, 26 and regulator 14” and concludes that “the vapor is inherently cooled by the carrier gas at outlet 4 because the carrier gas is at room temperature.”

Applicants respectfully disagree. Montgomery teaches that the embodiments in Figs. 3 and 4 are intended for different types of anesthetic agents. The embodiment of Fig. 4 is for use with an anesthetic agent that needs to be heated in order for it to vaporize. *See* Montgomery at col. 3, lines 14-18 (referring to Fig. 4, “when the boiling point of the anesthetic agent is about ambient temperature then to ensure pressure in the vaporizing chamber 12 a heater 32 is provided to raise the temperature of the anesthetic agent to above its boiling point.”). As discussed above, Montgomery teaches that when the anesthetic agent needs to be heated, passageways 6, 10, 26 and regulator 14 also need to be heated to prevent cooling of the vapor. *Id.* at col. 3, lines 18-25. By contrast, the embodiment of Fig. 3 is for use with an anesthetic agent does not need to be heated in order for it to vaporize. *See Id.* at col. 3, lines 6-10 (referring to Fig. 3, “for very low boiling point anesthetic agents, such as cyclopropane, with a boiling point of minus 32°C the pressure of the agent in the vaporizing chamber 12 at 22°C [*i.e.*, ‘room temperature’] can be very high, on the order of 75 psi.”). When the anesthetic agent vaporizes at room temperature, it is not “cooled” when it is mixed with a carrier gas that is also at room temperature.

Thus, even in the embodiment of Fig. 3, Montgomery fails to teach or suggest “cooling the resulting vapor by mixing the vapor with a gas” as required by claim 48 because, in that embodiment, the anesthetic agent is not heated and thus the resulting vapor is not cooled by mixing the vapor with a gas – both the resulting vapor and the gas are at room temperature. Thus, for this additional reason, the present invention is not anticipated by Montgomery.

In light of the above arguments and the amendment to claim 48, applicants respectfully request withdrawal of the rejection of claim 48 under 35 USC § 102(b), over Montgomery.

Claim Rejections Under 35 USC § 103

Claims 124-130 are rejected under 35 USC § 103(a) as being unpatentable over U.S. Patent No. 5,388,574, to Ingebrethsen (“Ingebrethsen”), in view of U.S. Patent No. 5,894,841, to Voges (“Voges”).

The Examiner cites Ingebrethsen as teaching “a method of generating aerosol comprising the steps of depositing a physiologically active compound ... onto a mesh screen carrier” and “heating the compound by passing a current across the carrier to vaporize the compound.” Office Action at 3. The Examiner acknowledges that “Ingebrethsen is silent with regards to the method comprising the step of mixing the vapor with the carrier gas in a ratio to form a desired particle size when a stable concentration of particles in the gas is reached.” *Id.* However, the Examiner asserts that “Voges teaches that the droplet size of an aerosol delivered to a patient is a function of the carrier gas pressure and velocity (col. 1, lines 43-55)” and concludes that “it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Ingebrethsen to include the step of mixing the resulting vapor with a carrier gas in a ratio to form a desired particle size since Voges teaches that it is well known in the art to control the particle size since the particle size is a function of the delivered pressure and velocity of the carrier gas, i.e., controlling the pressure and velocity of the carrier gas will alter the ratio of vapor to carrier gas and would produce aerosol with the same particle size, thus producing a stable concentration.” Office Action at 4.

Applicants respectfully disagree in view of the pending claims and the disclosures of Ingebrethsen and Voges. As amended, claim 124 is directed to: “A method of generating an aerosol comprising the steps of: (a) depositing a coating comprising a physiologically active compound onto an electrically conductive mesh screen; and (b) heating the coating by passing a current across the mesh screen to vaporize at least a portion of the compound, while simultaneously passing a gas through the mesh screen thereby mixing the resulting vapor with the gas in a predetermined ratio, selected to form an aerosol having a desired particle size when a stable concentration of particles in the gas is reached.”

By contrast, Ingebrethsen is directed to an aerosol delivery article that “provides delivery of aerosol particles of relatively small size without the necessity of exposing the material which is aerosolized to a significant degree of heat or high temperatures. An aerosol forming material is a multi-component material comprising an active ingredient and another ingredient having a

relatively low vaporization temperature, and preferably that aerosol forming material is in the form of an emulsion. The aerosol forming material is nebulized so as to provide first stage multi-component aerosol particles of fairly large size. The first stage aerosol particles then are subjected to heat so as to vaporize the other ingredient of that aerosol and cause further dispersion of that first stage aerosol. As such, a second stage aerosol composed of fine particles of active ingredient is provided.

The heating unit described in Ingebrethsen merely provides a heated region through which the “first stage” aerosol passes as it travels through the device (*see* Ingebrethsen, col. 2, line 65 - col. 3, line 9). Ingebrethsen states that “[t]ypically, the heating unit generates heat as a result of an electrical resistance heating unit element 72” which “can be provided by ... metal screens.” Ingebrethsen at col. 4, lines 21-23 & 29-32. However, Ingebrethsen does not teach depositing a coating comprising a physiologically active compound onto the electrical resistance heating unit. Rather, Ingebrethsen teaches “heating the air component” of the first stage aerosol, *e.g.*, as the aerosol travels through a heated passageway (*Id.* at col. 4, lines 41-54; col. 10, lines 36-38). In the preferred embodiment shown in Fig. 1, for example, the resistive heating element is provided by winding a resistance heating wire (72) around a coiled length of a tube (77) through which the aerosol passes. *See Id.* at col. 4, lines 37-39. Ingebrethsen states that the heating unit should have “a surface area and configuration so that a significant amount of the aerosol particles does not experience contact with components of the heating unit” to avoid deposition of the particulate material (Ingebrethsen, col. 10, line 56 - col. 11, line 2). Thus, Ingebrethsen does not teach or suggest “depositing a coating comprising a physiologically active compound onto an electrically conductive mesh screen” as required by claim 124; in fact, Ingebrethsen teaches against depositing a physiologically active compound onto an electrically conductive mesh screen. As such, Applicants’ claimed invention is clearly distinguishable over the teachings of Ingebrethsen.

Voges does not cure the deficiencies of Ingebrethsen. Voges pertains to a dispenser comprising a reservoir of a physiologically active substance and a droplet ejection device which is controlled to issue a predetermined number of discrete droplets of the substance from ejection orifices upon actuation (Voges, abstract). However, the passage cited by the Examiner relates to jet nebulizers that generate an aerosol by atomizing a liquid in a carrier gas stream and merely states that the droplet size of the resulting aerosol is a function of carrier gas pressure and

velocity. This teaching with respect to the effect carrier gas pressure and velocity have on droplet size in jet nebulizers (where liquid is fragmented by shear force to form droplets) is not applicable to the invention claimed by Applicants where a vapor is mixed with a gas, in a ratio, to form an aerosol having a desired particle size, as disclosed and claimed by applicants. Voges does not teach or suggest the series of method steps disclosed and claimed by applicants. As such, applicants' claimed invention is clearly distinguishable over the teachings of Ingebrethsen. As stated above, Ingebrethsen teaches away from Applicants' claimed invention. Therefore, even if one were to combine the teachings of Voges with those of Ingebrethsen, one skilled in the art would not be led to make Applicants' invention.

Whether taken alone or in combination, neither Ingebrethsen nor Voges teaches or even suggests Applicants' claimed invention. In light of the above arguments, Applicants respectfully request withdrawal of the rejection of claims 124-130 under 35 USC § 103(a), over Ingebrethsen, in view of Voges.

Claims 181-186 and 188-196 are rejected under 35 USC § 103(a) as being unpatentable over Montgomery, as applied to claim 48 in view of Voges.

As discussed above, Montgomery fails to teach or suggest "form[ing] an aerosol" as required by claim 48, upon which claims 181-186 and 188-196 depend. In addition, as discussed above, Montgomery fails to teach or suggest the limitation of "cooling the resulting vapor by mixing the vapor with a gas" as also required by claim 48. In fact, Montgomery teaches away from cooling the resulting vapor.

Voges does not cure the deficiencies of Montgomery. As discussed above, Voges pertains to a dispenser comprising a reservoir of a physiologically active substance and a droplet ejection device which is controlled to issue a predetermined number of discrete droplets of the substance from ejection orifices upon actuation, and its teaching with respect to the effect carrier gas pressure and velocity have on droplet size in jet nebulizers (where liquid is fragmented by shear force to form droplets) is not applicable to the invention claimed by Applicants where a vapor is mixed with a gas, in a ratio, to form an aerosol having a desired particle size, as disclosed and claimed by Applicants.

Whether taken alone or in combination, neither Montgomery nor Voges teaches or even suggests Applicants' claimed invention. In light of the above arguments, Applicants respectfully

request withdrawal of the rejection of claims 124-130 under 35 USC § 103(a), over Montgomery, in view of Voges.

Claim 187 is rejected under 35 USC § 103(a) as being unpatentable over Montgomery, as applied to claim 48 in view of Voges and further in view of U.S. Patent No. 5,874,841 (“Weers et al.”).

The Examiner states that the combination of Montgomery/Voges is silent with regards to the particle size in the range of 10 nm to 100 nm. However, the Examiner asserts that “Weers et al. teaches that is known in the respiratory art to have particle sizes in the range of 10 nm to 100 nm” and concludes that “it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the steps taught by the above combination to include the particle size range of 10 to 100 nm since Weers et al. teaches that the recited range is known in the art and would be dependent upon the intended therapy.” Office Action at 7-8.

Applicants respectfully disagree. Claim 187 is not obvious over Montgomery, as applied to claim 48 in view of Voges for the same reasons described above with respect to claims 181-186 and 188-196. Weers et al. does not cure these deficiencies. Weers et al. relates to thermodynamically stable molecular solutions providing enhanced bioavailability for lipophilic pharmaceutical agents (Weers et al., abstract). The passage cited by the Examiner regarding particle sizes in the range of 10 to 100 nm relates to formulations for oral administration, not to aerosols. See *Id.* at col. 5, lines 4-8 (“For oral administration, smaller drug particles or crystals, often on the order of 10 nm to 100 nm with large surface areas, are preferred due to their rapid diffusion for the delivery vehicle to the site of action.”). Weers et al. does not teach or suggest how to make an aerosol having particles in that size range. In addition, Weers et al. does not disclose or suggest “cooling the resulting vapor by mixing the vapor with a gas, in a ratio, to form an aerosol.”

Whether taken alone or in combination, Montgomery, Voges and Weers et al. do not teach or even suggest Applicants’ claimed invention. In light of the above arguments, Applicants respectfully request withdrawal of the rejection of claim 187 under 35 USC § 103(a), over Montgomery, in view of Voges and further in view of Weers et al.

Closing Remarks

Applicants appreciate the Examiner's careful and thorough review of the application and submit that the Examiner's concerns have been addressed by the amendments and remarks above. Applicants accordingly request that the Examiner withdraw all rejections and allow the application. In the event that the Examiner believes that a telephonic discussion would expedite allowance or help to resolve outstanding issues in the prosecution of the application, the Examiner is invited to call the undersigned at the telephone number set forth below.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Applicants respectfully request reconsideration of the application, withdrawal of all rejections, and allowance of the application in view of the amendments and remarks set forth above.

Respectfully submitted,

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